7/7/12
DIALOG(R)File 155:MEDLINE(R)

06924727 91237836 PMID: 2033669
Origin of adeno-associated virus DNA replication is a target of carcinogen-inducible DNA amplification.
Yalkinoglu A O; Zentgraf H; Hubscher U
Institut fur Virusforschung/Angewandte Tumorvirologie, Deutsches Krebsforschungszentrum, Heidelberg, Federal Republic of Germany.
Journal of virology (UNITED STATES) Jun 1991, 65 (6) p3175-84, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
DNA amplification of the helper-dependent parvovirus AAV (adeno-associated virus) can be induced by a variety of genotoxic agents in the absence of coinfecting helper virus. Here we investigated whether the origin of AAV type 2 DNA replication cloned into a plasmid is sufficient to promote replication activity in cells treated by the carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG). A pUC19-based plasmid, designated pA2Y1, which contains the left terminal repeat sequences (TRs) representing the AAV origin of replication and the p5 and p19 promoter but lacks any functional parvoviral genes is shown to confer replication activity and to allow selective DNA amplification in carcinogen-treated cells. Following transfection of plasmid pA2Y1 or plasmid pUC19 as a control, density labeling by a bromodeoxyuridine and DpnI resistance assay suggested a semi-conservative mode of replication of the AAV origin-containing plasmid. Furthermore, the amount of DpnI-resistant full-length pA2Y1 DNA molecules was increased by MNNG treatment of cells in a dose-dependent manner. In addition, DNA synthesis of plasmid pA2Y1 was studied in vitro. Extracts derived from MNNG-treated CHO-9 and L1210 cells displayed greater synthesis of DpnI-resistant full-length pA2Y1 molecules than did nontreated controls. Experiments with specific enzyme inhibitors suggested that the reaction is largely dependent on DNA polymerase alpha, DNA primase, and DNA topoisomerase I. Furthermore, restriction endonuclease mapping analysis of the in vitro reaction products revealed the occurrence of specific initiation at the AAV origin of DNA replication. Though elongation was not very extensive, extracts from carcinogen-treated cells markedly amplified the AAV origin region. Our results, including electron microscopic examination, suggest that the AAV origin/terminal repeat structure is recognized by the cellular DNA replicative machinery induced or modulated by carcinogen treatment in the absence of parvoviral gene products.
Record Date Created: 19910626
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4/7/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06701124 91012793 PMID: 2145445

Interaction of virally coded protein and a cell cycle-regulated cellular protein with the bovine parvovirus left terminus ori.

Metcalf J B; Bates R C; Lederman M

Biology Department, Virginia Polytechnic Institute and State University, Blacksburg 24061-0406.

Journal of virology (UNITED STATES) Nov 1990, 64 (11) p5485-90, ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Replication of parvoviruses requires cis signals located in terminal palindromes that function as origins of replication in conjunction with trans-acting viral and cellular proteins. A gel retardation assay was used to identify proteins in crude nuclear extracts of bovine parvovirus (BPV)-infected bovine fetal lung cells that interact with the hairpinned left end (3' OH terminus of the viral minus strand in the flop conformation) of BPV. Three specific DNA-protein complexes formed. One complex was shown to involve a BPV structural protein(s) by inhibiting its formation when antiserum specific for these BPV proteins was used. By specific competition with serum containing antibodies against the BPV nonstructural proteins, a second complex was shown to involve a BPV nonstructural protein. A third complex contained protein of cellular origin and was also formed with extracts of uninfected bovine fetal lung cells. DNA competition assays suggest that the viral proteins do not bind to the right hairpin, which differs in sequence and secondary structure from the left terminus, or to a BPV terminus that lacks the first 52 nucleotides, preventing formation of the stem of the hairpin. The cellular protein is regulated in a cell cycle-dependent fashion, with its binding activity increased in uninfected, actively dividing cells compared with contact-inhibited cells. Since autonomous parvovirus replication requires an S-phase factor for progeny formation, the terminal binding protein demonstrated here is a candidate for this factor.

Record Date Created: 19901115

7/7/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03186483 80001961 PMID: 225040
Structure of the 3' hairpin termini of four rodent parvovirus genomes: nucleotide sequence homology at origins of DNA replication.
Astell C R; Smith M; Chow M B; Ward D C
Cell (UNITED STATES) Jul 1979, 17 (3) p691-703, ISSN 0092-8674
Journal Code: 0413066
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The nucleotide sequences of the 3' termini of the DNA from four autonomous rodent parvoviruses have been determined. The terminus of each genome exists as a Y-shaped hairpin structure involving 115 or 116 nucleotides. The sequence of this region of DNA is highly conserved and shows no evidence of internal sequence heterogeneity, a characteristic which is observed in the terminal nucleotide sequence of the helper-dependent, adeno-associated viruses (Berns et al., 1978a). The implications of these results with respect to the models of parvovirus DNA replication are discussed.
Record Date Created: 19791129

4/7/45 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0209359 DBR Accession No.: 97-04480 PATENT
Recombinant vectors based on parvo virus nucleic acids - parvo virus vector for use in cancer gene therapy
AUTHOR: Rhode S L; Maxwell F
CORPORATE SOURCE: USA.
PATENT ASSIGNEE: Univ.Colorado-Found. 1996
PATENT NUMBER: US 5585254 PATENT DATE: 961217 WPI ACCESSION NO.: 97-064348 (9706)
PRIORITY APPLIC. NO.: US 685628 APPLIC. DATE: 910415
NATIONAL APPLIC. NO.: US 685628 APPLIC. DATE: 910415
LANGUAGE: English
ABSTRACT: A recombinant vector contains nucleic acid sequences of an autonomous parvo virus (AP) joined to at least 1 foreign nucleic acid sequence. The AP sequences comprise functional left and right end inverted terminal repeats enclosing the foreign sequence, which is located between them. Also claimed are: a recombinant virus particle comprising a vector packaged in an autonomous parvo virus capsid; a helper construct plasmid pSVLu; and a method for producing a recombinant virus particle for delivery of a gene to a targeted cell, which involves cotransfecting a host cell with a vector and a helper construct that effects amplification of the vector and/or packaging of the vector in a parvo virus capsid and culturing the transfected host cell. The vector is used as a delivery vehicle for gene therapy, especially for restoring the function of a defective gene or for expressing a cytotoxic agent to destroy cancer cells or pathogen-infected cells and for production of the RNA or protein encoded by the heterologous nucleic acid sequence (all claimed). (26pp)

05670611 88091050 PMID: 3275788

Genomic clones of bovine parvovirus: construction and effect of deletions and terminal sequence inversions on infectivity.

Shull B C; Chen K C; Lederman M; Stout E R; Bates R C

Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061-0794.

Journal of virology (UNITED STATES) Feb 1988, 62 (2) p417-26, ISSN 0022-538X Journal Code: 0113724

Contract/Grant No.: RRO-7095; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Genomic clones of the autonomous parvovirus bovine parvovirus (BPV) were constructed by blunt-end ligation of reannealed virion plus and minus DNA strands into the plasmid pUC8. These clones were stable during propagation in Escherichia coli JM107. All clones tested were found to be infectious by the criteria of plaque titer and progressive cytopathic effect after transfection into bovine fetal lung cells. Sequencing of the recombinant plasmids demonstrated that all of the BPV inserts had left-end (3')-terminal deletions of up to 34 bases. DNA isolated from progeny virions arising from transfected infectious clones was found to be indistinguishable from wild-type DNA by restriction enzyme analysis. Defective genomes could also be detected in the progeny DNA even though the infection was initiated with homogenous, cloned DNA. Full-length genomic clones with 3' flip and 3' flop conformations were constructed and were found to have equal infectivity. Analysis of low-molecular-weight DNA isolated from lysates of cells transfected with these clones demonstrated that rescue and replication of BPV DNA could be detected 3 to 8 days after transfection. Expression of capsid proteins from transfected genomes was demonstrated by hemagglutination, indirect immunofluorescence, and immunoprecipitation of [35S]methionine-labeled cell lysates. Use of appropriate antiserum for immunoprecipitation showed the synthesis of BPV capsid and noncapsid proteins after transfection. Independently, a series of genomic clones with increasingly larger 3'-terminal deletions was prepared from separately subcloned 3'-terminal fragments. Transfection of these clones into bovine fetal lung cells revealed that deletions of up to 34 bases at the 3' end lowered but did not abolish infectivity, while deletions of greater than 52 bases were lethal. End-label analysis showed that the 34-base deletion was repaired to wild-type length in the progeny virus.

Record Date Created: 19880220

07865779 94002366 PMID: 8399491

Recombinant LuIII autonomous parvovirus as a transient transducing vector for human cells.

Maxwell I H; Maxwell F; Rhode S L; Corsini J; Carlson J O
University of Colorado Cancer Center, Denver 80262.

Human gene therapy (UNITED STATES) Aug 1993, 4 (4) p441-50, ISSN 1043-0342 Journal Code: 9008950
Contract/Grant No.: CA50285; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Recombinants based on the genome of the autonomous parvovirus, LuIII, were constructed by replacing the viral coding sequences in an infectious clone (pGLu883) by a luciferase or beta-galactosidase reporter, which was linked to the viral P4 promoter. In cells cotransfected with either of these constructs, together with a plasmid supplying LuIII nonstructural and capsid proteins, excision and replication of the recombinant genome occurred. Transducing virions accumulated in the culture medium of the cotransfected cells, as assayed by reporter activity in recipient cells exposed to this medium. Transducing activity could be neutralized by antiserum to LuIII. Production of replicative form DNA and transducing virions were observed following cotransfection of HeLa, 293, or NB324K cells, in increasing order of efficiency. When homology existed between the recombinant genome and sequences flanking the viral genes in the helper construct, concomitant production of replication-competent, cytopathic virus was sometimes observed. This could be minimized by removal of the left end homology from the helper; by this means, preparations of luciferase transducing virus were obtained free from replication-competent virus. With such preparations, we observed luciferase expression (declining after 3 days) for up to 7 days in recipient HeLa cells. Hybridization of the recombinant viral DNA with strand-specific luciferase probes indicated packaging of both strands (as reported for LuIII), but with a several-fold excess of the (-) strand. We suggest that transducing-autonomous parvoviruses will be useful in gene transfer applications, possibly including gene therapy when only transient expression is desired.

Record Date Created: 19931123

~~1029~~ No-priority doc, in Eng 854

4/7/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10378075 99355161 PMID: 10428207

cis requirements for the efficient production of recombinant DNA vectors based on autonomous parvoviruses.

Kestler J; Neeb B; Struyf S; Van Damme J; Cotmore S F; D'Abramo A; Tattersall P; Rommelaere J; Dinsart C; Cornelis J J

Applied Tumor Virology Abt. F0100 and INSERM U375 Deutsches Krebsforschungszentrum, Heidelberg, Germany.

Human gene therapy (UNITED STATES) Jul 1 1999, 10 (10) p1619-32, ISSN 1043-0342 Journal Code: 9008950

Contract/Grant No.: CA29303; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The replication of viral genomes and the production of recombinant viral vectors from infectious molecular clones of parvoviruses MVMp and H1 were greatly improved by the introduction of a consensus NS-1 nick site at the junction between the left-hand viral terminus and the plasmid DNA. Progressive deletions of up to 1600 bp in the region encoding the structural genes as well as insertions of foreign DNA in replacement of those sequences did not appreciably affect the replication ability of the recombinant H1 virus genomes. In contrast, the incorporation of these genomes into recombinant particles appeared to depend on in cis-provided structural gene sequences. Indeed, the production of H1 viral vectors by cotransfection of recombinant clones and helper plasmids providing the structural proteins (VPs) in trans, drastically decreased when more than 800 bp was removed from the VP transcription unit. Furthermore, titers of viral vectors, in which most of the VP-coding region was replaced by an equivalent-length sequence consisting of reporter cDNA and stuffer DNA, were reduced more than 50 times in comparison with recombinant vectors in which stuffer DNA was not substituted for the residual VP sequence. In addition, viral vector production was restricted by the overall size of the genome, with a mere 6% increase in DNA length leading to an approximately 10 times lower encapsidation yield. Under conditions fulfilling the above-mentioned requirements for efficient packaging, titers of virus vectors from improved recombinant molecular DNA clones amounted to 5 x 10(7) infectious units per milliliter of crude extract. These titers should allow the assessment of the therapeutic effect of recombinant parvoviruses expressing small transgenes in laboratory animals.

Record Date Created: 19990922

5/7/10
DIALOG(R)File 155:MEDLINE(R)

08200448 94335120 PMID: 8057478
Adeno-associated virus DNA replication in vitro: activation by a maltose binding protein/Rep 68 fusion protein.
Ward P; Urcelay E; Kotin R; Safer B; Berns K I
Department of Microbiology, Hearst Microbiology Research Center, Cornell University Medical College, New York, New York 10021.
Journal of virology (UNITED STATES) Sep 1994, 68 (9) p6029-37, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: GM 50032; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The adeno-associated virus (AAV) nonstructural protein Rep 68 is required for viral DNA replication. An in vitro assay has been developed in which addition of Rep 68 to an extract from uninfected HeLa cells supports AAV DNA replication. In this paper, we report characterization of the replication process when a fusion of the maltose binding protein and Rep 68, expressed in Escherichia coli, was used in the assay. Replication was observed when the template was either linear double-stranded AAV DNA or a plasmid construct containing intact AAV DNA. When the recombinant plasmid construct was used as the template, there was replication of pBR322 DNA as well as the AAV DNA; however, linear pBR322 DNA was not replicated. When the plasmid construct was the template, replication appeared to initiate on the intact plasmid and led to separation of the AAV sequences from those of the vector, a process which has been termed rescue. There was no evidence that replication could initiate on the products of rescue. Rep 68 can make a site-specific nick 124 nucleotides from the 3' end of AAV DNA; the site of the nick has been called the terminal resolution site. Our data are most consistent with initiation occurring at the terminal resolution site and proceeding toward the 3' terminus. When the template was the plasmid construct, either elongation continued past the junction into pBR322 sequences or the newly synthesized sequence hairpinned, switched template strands, and replicated the AAV DNA. Replication was linear for 4 h, during which time 70% of the maximal synthesis took place. An additional finding was that the Rep fusion could resolve AAV dimer length duplex intermediates into monomer duplexes without DNA synthesis.
Record Date Created: 19940909

5/7/10
DIALOG(R)File 155:MEDLINE(R)

08200448 94335120 PMID: 8057478
Adeno-associated virus DNA replication in vitro: activation by a maltose binding protein/Rep 68 fusion protein.
Ward P; Urcelay E; Kotin R; Safer B; Berns K I
Department of Microbiology, Hearst Microbiology Research Center, Cornell University Medical College, New York, New York 10021.
Journal of virology (UNITED STATES) Sep 1994, 68 (9) p6029-37, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: GM 50032; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
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Record Date Created: 19940909

5/7/10
DIALOG(R)File 155:MEDLINE(R)

08200448 94335120 PMID: 8057478
Adeno-associated virus DNA replication in vitro: activation by a maltose binding protein/Rep 68 fusion protein.
Ward P; Urcelay E; Kotin R; Safer B; Berns K I
Department of Microbiology, Hearst Microbiology Research Center, Cornell University Medical College, New York, New York 10021.
Journal of virology (UNITED STATES) Sep 1994, 68 (9) p6029-37, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: GM 50032; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The adeno-associated virus (AAV) nonstructural protein Rep 68 is required for viral DNA replication. An in vitro assay has been developed in which addition of Rep 68 to an extract from uninfected HeLa cells supports AAV DNA replication. In this paper, we report characterization of the replication process when a fusion of the maltose binding protein and Rep 68, expressed in Escherichia coli, was used in the assay. Replication was observed when the template was either linear double-stranded AAV DNA or a plasmid construct containing intact AAV DNA. When the recombinant plasmid construct was used as the template, there was replication of pBR322 DNA as well as the AAV DNA; however, linear pBR322 DNA was not replicated. When the plasmid construct was the template, replication appeared to initiate on the intact plasmid and led to separation of the AAV sequences from those of the vector, a process which has been termed rescue. There was no evidence that replication could initiate on the products of rescue. Rep 68 can make a site-specific nick 124 nucleotides from the 3' end of AAV DNA; the site of the nick has been called the terminal resolution site. Our data are most consistent with initiation occurring at the terminal resolution site and proceeding toward the 3' terminus. When the template was the plasmid construct, either elongation continued past the junction into pBR322 sequences or the newly synthesized sequence hairpinned, switched template strands, and replicated the AAV DNA. Replication was linear for 4 h, during which time 70% of the maximal synthesis took place. An additional finding was that the Rep fusion could resolve AAV dimer length duplex intermediates into monomer duplexes without DNA synthesis.
Record Date Created: 19940909

04676844 85058177 PMID: 6094825

Replication of adeno-associated virus DNA. Complementation of naturally occurring rep- mutants by a wild-type genome or an ori- mutant and correction of terminal palindrome deletions.

Senapathy P; Tratschin J D; Carter B J

Journal of molecular biology (ENGLAND) Oct 15 1984, 179 (1) p1-20, ISSN 0022-2836 Journal Code: 2985088R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

When the entire adeno-associated virus (AAV) genome is inserted into a bacterial plasmid, infectious AAV genomes can be rescued and replicated when the recombinant AAV-plasmid DNA is transfected into human 293 cells together with helper adenovirus particles. We have taken advantage of this experimental system to analyze the effects of several classes of mutations on replication of AAV DNA. We obtained AAV mutants by molecular cloning in bacterial plasmids of naturally occurring AAV variant or defective-interfering genomes. Each of these mutants contains a single internal deletion of AAV coding sequences. Also, some of these mutant-AAV plasmids have additional deletions of one or both AAV terminal palindromes introduced during constructions in vitro. We show here that AAV mutants containing internal deletions were defective for replicative form DNA replication (rep-) but could be complemented by intact wild-type AAV. This indicates that an AAV replication function, Rep, is required for normal AAV replication. Mutants in which both terminal palindromes were deleted (ori-) were also replication defective but were not complementable by wild-type AAV. The cis-dominance of the ori- mutation shows that the replication origin is comprised in part of the terminal palindrome. Deletion of only one terminal palindrome was phenotypically wild-type and allowed rescue and replication of AAV genomes in which the deleted region was regenerated apparently by an intramolecular correction mechanism. One model for this correction mechanism is proposed. An AAV ori- mutant also complemented replication of AAV rep- mutants as efficiently as did wild-type AAV. These studies also revealed an unexpected additional property of the deletion mutants in that monomeric single-stranded single-stranded DNA accumulated very inefficiently even though monomeric single-stranded DNA from the complementing wild-type AAV did accumulate.

Record Date Created: 19841228